

REMARKS/ARGUMENTS

Claims that stand withdrawn are hereby cancelled without prejudice of later re-introduction, or prosecution through appropriate continuation/divisional practice. Pending claims are respectfully submitted as being subject to linking claim practice.

New claims 36-38 are hereby introduced. These claims comprise recitation of original dependent claims 7, 14, and 17 with limitations from the corresponding intervening claims. Claims 36-38 should presently be in allowable condition in light of the objections asserted in the Office Action with respect to original claims 7, 14, and 17.

The correction as to language required in the Office Action in claim 1 has been hereby introduced by claim amendment. This correction merely introduces an inadvertently omitted conjunction and thus represents no narrowing amendment to such claim and its dependent claims.

Rejections under 35 U.S.C. § 102(b) are asserted in the Office Action in light of U.S. Pat. No. 5,612,016 to Griffiths, *et al.* (hereinafter the '016 patent"), and an interpretation of part of the claim recitation that consists of the language "apo metal binding protein". Applicants respectfully submit that such terms do not read on the '016 patent for at least the following reasons.

Whereas claim language is to be given the broadest reasonable meaning, such meaning is to be given in light of the specification. Applicants respectfully submit that neither the quoted definition of the terms "apo metal binding protein" nor the specification as a whole, support the reading of such terms as referring to a protein that requires its conjugation with a chelating agent in order to participate in a binding with a metal. However, this is the requirement of the proteins disclosed in the '016 patent. In contrast, the terms "apo metal binding protein" in the present

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claims are supported by a description that at all times refers to proteins that by themselves bind to a metal.

The '016 patent describes, as noted in the Office Action, proteins that must be conjugated to a chelating agent, so that such chelating agent, when conjugated to the protein, can bind to a metal. The '016 patent describes chelating agents and also the step of conjugating such chelating agents to proteins to generate a protein-chelating agent conjugated unit in which the metal chelate is formed with the conjugated chelating agent, not with the protein.

The definition of "apo metal binding protein" from the present specification that is quoted in the Office Action refers to any protein or peptide that, *inter alia*, binds itself to a metal. In contrast, the '016 patent describes a protein that is to be conjugated to a chelating agent so that such chelating agent in the conjugated protein-agent entity can bind to a metal, rather than the non-conjugated protein itself.

Furthermore, the direct use of the protein itself as described in the present specification is in contrast with the conjugation of the protein with the chelating agent and the subsequent use of the ensuing conjugated entity that is described in the '016 patent. The examples given in the present application also are in marked contrast with the description provided in the '016 patent.

The '016 patent does not disclose proteins that are capable by themselves to bind to a metal, absent conjugation with a chelating agent. The quoted definition of "apo metal binding protein" clearly refers to proteins that exhibit certain behavior upon themselves binding to a metal, a characteristic that the proteins described in the '016 patent do not have. Therefore, the pending claims do not read on the proteins described in the '016 patent. Because the pending claims do not read on embodiments in which the protein does not bind to the metal, as described in the '016 patent, such patent may not anticipate the pending claims.

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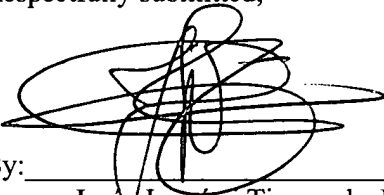
Applicants respectfully request that the rejections under 35 U.S.C. § 102(b) be withdrawn.

The rejections that are asserted in the Office Action under 35 U.S.C. § 103(a) rely on the '106 patent and on the same interpretation of the claim language recitation as discussed in the context of the rejections under 35 U.S.C. § 102(b). For at least the same reasons set forth hereinabove, Applicants respectfully submit that the '106 patent may not render obvious the present claims. Furthermore, the '106 patent does not suggest or provide a motivation for the claimed methods because problems that are solved by the claimed methods, such as problems derived from extra manipulations, are not addressed by the methods described in the '106 patent. In addition, reliance on protein-chelating agent conjugation as in the '106 is not necessitated by the claimed methods.

Applicants respectfully request that the rejections under 35 U.S.C. § 103(a) be withdrawn.

Applicants respectfully request that a timely Notice of Allowance be issued in this case.

Respectfully submitted,


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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

1. (Once Amended) A method of monitoring at least one target substance in a biological system comprising:
 - a) providing said biological system comprising said at least one target substance;
 - b) labeling said at least one target substance with at least one apo metal binding protein;
 - c) providing conditions which permit said at least one apo metal binding protein to emit a signal;
 - d) observing or measuring the signal; and
 - e) monitoring said at least one target substance based on the signal observed or measured.

17. (Once Amended) The method of claim 15, wherein said [copper] apo metal binding protein is [a blue copper protein] chosen from azurin, pseudo-azurin, a plastocyanin, and a phytocyanin.